UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

MJ

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/336,266	06/14/99	BEMIS	

EXAMINER	
G	VPI/96-16.CI

ART UNIT	PAPER NUMBER
1624	7

HM12/0911

JAMES F HALEY JR
FISH & NEAVE
1251 AVENUE OF THE AMERICAS
NEW YORK NY 10020

RAO,D

DATE MAILED: 09/11/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/336,266	Bemis et al.
Examiner	**Group Art Unit**
Deepak Rao	1624

☒ Responsive to communication(s) filed on *Apr 4, 2000*

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *4-12, 15, and 18-38* is/are pending in the applicat

Of the above, claim(s) _____ is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *4-12, 15, and 18-38* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *4*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

This office action is in response to the amendment filed on April 4, 2000. Claims 1-3, 13-14 and 16-17 are canceled by the amendment and new claim 38 is added.

Claims 4-12, 15 and 18-38 are currently pending in this application.

Election/Restriction

Applicant's election of Group X in Paper No. 6 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Applicant's election of the species of compound no. 407 (specification page 50) is also acknowledged. As the elected species was not found in the prior art, the search was expanded to the genus of the elected invention of Group X.

Priority

It is acknowledged that the instant application is a continuation of PCT/US97/23392 filed December 17, 1997 which claims the benefit of provisional application no. 60/034,288 filed December 18, 1996. The first paragraph in the specification currently does not contain the information of the parent applications. Reference to all parent application(s) including PCT and the provisional applications is required, see MPEP § 201.11.

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 38, 4-12, 15, 18-21 and 25-37 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the compounds of formulae (Ie), (If), (Ig) and (Ih) wherein Q_1 is phenyl or pyridyl groups, Q_2 is phenyl, thienyl, benzofuran, benzothiophene or indolyl and Q_3 is phenyl (all of which are unsubstituted or substituted), does not reasonably provide enablement for other definitions provided for Q_1-Q_3. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

1. The specification provides no sufficient enabling disclosure by way of representative examples or reasonable disclosure of starting material sources for the plethora of functional groups permitted at all Q_1, Q_2 and Q_3 variables which include various cyclic moieties both carbocyclic and heterocyclic. Additionally preparation of only compounds carrying phenyl/pyridyl/thienyl/indolyl rings are disclosed in the specification. Such diverse embodiments have not been shown by adequate representation to be applicant's invention. Specification is silent about the availability of necessary reactants needed to prepare such a scope and does not particularly teach the means by which they may be

prepared. See *Ex parte Moersch*, 104 USPQ 122; *In re Howarth*, 210 USPQ 689; *In re Lund*, 153 USPQ 625; *In re Wiggins*, supra.

2. Further, there is no reasonable basis for assuming that the myriad of compounds embraced by the claims will all share the same physiological properties since they are so structurally dissimilar as to be chemically non-equivalent and there is no basis in the prior art (directed to p38 inhibitors) for assuming the same. Note *In re Surrey*, 151 USPQ 724 regarding sufficiency of disclosure for a Markush group. Also see MPEP § 2164.03 for enablement requirements in cases directed to structure-specific arts such as the pharmaceutical art. The only exemplified compounds made (see Tables 3-5) are so different from the compounds embraced by the genus such that no reasonable extrapolation could be made by one skilled in the art regarding the activity of the compounds. Receptor activity is generally unpredictable and highly structure specific area.

3. Furthermore, the scope of the method claims 26-37, is not adequately enabled solely based on p38 inhibitory activity provided in the specification. The instant claims are drawn to 'a method of .... **preventing**...' diseases such as neurodegenerative diseases including Alzheimer's disease, viral diseases including HIV infection, etc., and therefore, the instant claim language embraces disorders not only for the treatment, but for "prevention" which is not remotely enabled. The instant compounds are disclosed have p38 inhibitory activity and it is recited that the instant compounds are useful in the "prevention" of Alzheimer's disease, HIV infection, heart attacks, etc., for which applicants provide no competent

evidence. "To prevent" actually means *to anticipate* or *counter in advance, to keep from happening etc.* (as per Websters II Dictionary) and therefore it is not understood how one skilled in the art can reasonably establish the basis and the type of subject to which the instant compounds can be administered in order to have the "prevention" effect. The specification provides assays for the inhibition of p38, ATPase, IL-1, IL-6, IL-8, TNF and COX-2, which relate to mostly inflammatory mechanism. Thus, it is inconceivable as to how the claimed compounds can not only treat but also "prevent" a myriad of diseases with different etiologies. For example, a viral disease such as HIV infection has been known to be treated with a nucleoside analog or a protease inhibitor to disrupt the production of viral protein or DNA. Also, neurodegenerative disease such as Alzheimer's disease has no known cause and has been treated mostly by choline esterase inhibitors to prolong the activity of acetylcholine. A disease such as myocardial ischemia mostly relates to the deposition of plague in the coronary artery. (Only a few of the claimed diseases are discussed here to make the point of an insufficient disclosure, it does not definitely mean that the other diseases meet the enablement requirements). There is no evidence of record which would enable the skilled artisan in the identification of the people who have the potential of becoming afflicted with the disease(s) or disorder(s) claimed herein.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 38, 4-12, 15 and 18-37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

1. In claim 38, the structural representation of formulae (Ie), (If), (Ig) and (Ih) have nodes that overlap with the bonds and therefore, are not clearly comprehensible. Clear representation of the structures (as in page 35 of the specification) is required. Further, it appears that formulae (Ie)-(If) and (Ig)-(Ih) have been interchanged in the claim (i.e., formula (Ie) in the specification page 35 is indicated as formula (If) in the claim, etc.).
2. In claim 38, Q_1-Q_3 are defined to be "heterocyclic" ring systems, however, the number and types of heteroatoms involved in these ring systems is not adequately set forth. The specification does not provide any definition for this term. See *In re Wiggins*, 179 USPQ 421 regarding such terminology.
3. In claim 38, page 4, third line from the bottom of the page, there is a period (.) following R^3. Each claim must begin with a capital letter and end with a period, periods may not be used any where else in the claim. See MPEP § 608.01(m).
4. In claim 38, page 5, lines 2-3, a definition is provided for " R_1 ", however, such variable was not found to be present in the structural formulae or in the definitions of other variables.
5. In claim 6, pages 115-116, a number of structures show "O" and "N" which are substituted on the phenyl ring, having open valencies, see the fourth structure on line 4,

first and second structures on line 5, etc. Further, the nitrogen at 4-position of the piperazine ring also has an open valency. The specification on pages 10-11 also discloses several structures having the same problem.

6. Claim 7 recites the limitation "2-chloro-4-hydroxyphenyl, 2-chloro-4-aminophenyl" in lines 3-4. There is insufficient antecedent basis for this limitation in claim 6 on which claim 7 is dependent. (Claim 6 leaves the O and/or N open in the structures and therefore, it is unclear what is represented by many of the formulae, see reason no. 4 above).

7. Claim 11 recites the limitation "X is selected from ..... **-NR-, -C(R_2)-...**" in lines 3-4. There is insufficient antecedent basis for this limitation in claim 38 on which claim 11 is dependent. Claim 38 defines X to be -N(R^2)-, -C(R^2)$_2$-, etc. The terminology should be consistent through out the claims.

8. In claim 18, lines 4-5, the phrase "to the rest of the inhibitor" is not understood. Claim 38 is drawn to 'A compound' and therefore, it is confusing what is being referred by "the inhibitor".

9. Claim 22 is drawn species representing formula (Ie), however, the claim does not show the species claimed and refers to the specification. A claim to be complete must include all the limitations within the claim. Further, the formula (Ie) in claim 38 is different from that of the specification.

10. Claim 23, drawn to the species of formula (Ig), does not show the compounds and refers to the specification. (See reason no. 8 above).

11. Claim 24, drawn to the species of formula (Ih), does not show the claimed species but refers to the specification. (See reason no. 8 above).

12. Claim 26 drawn to a method, lists 'inflammatory diseases' as well as 'allergies' in the list of disorders. Dependent claim 27 recites 'allergies' as a subset of 'inflammatory diseases', which is confusing and unclear. Are the 'allergies' recited in claim 26 different from those of claim 27? The specification does not provide any help.

13. Claim 32 recites the limitation "a viral disease" in line 2. There is insufficient antecedent basis for this limitation in claim 26 on which claim 32 is dependent. It is not clear which of the diseases recited in claim 26 are associated with the instantly recited viral diseases.

14. Claim 34 recites the limitation "myocardial ischemia, renal ischemia" in lines 3-4. There is insufficient antecedent basis for this limitation in claim 26 on which claim 34 is dependent. These terms are not recited in claim 26 and it is not clear which diseases are these terms associated with.

15. Claim 35 recites the term "endoperoxide" in line 3. There is insufficient antecedent basis for this term in claim 26 on which claim 35 is dependent. Claim 26 recites 'endoperoxidase', see line 8.

The claims not particularly addressed are included here because they are dependent claims and do not resolve the above issues.

Receipt is acknowledged of the Information Disclosure Statement filed on April 4, 2000 and a copy is enclosed herewith.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Rao whose telephone number is (703) 305-1879. The fax phone number for this Group is (703) 308-4556. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group Receptionist whose telephone number is (703) 308-1235.

Mukund J. Shah

Mukund J. Shah
Supervisory Patent Examiner
Art Unit 1624

Deepak Rao
September 6, 2000